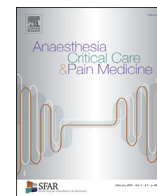




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Letter to the Editor

Association of ABO blood group with indices of disease severity and multiorgan dysfunction in COVID-19**Keywords:**

ARDS
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News – Score
Intensive care unit

Dear Editor,

We read with great interest the work by Hoiland et al. [1], which suggests a strong correlation between ABO blood group and severity of COVID-19. One striking message of this study is that critically ill COVID-19 patients with blood group A or AB are at increased risk for mechanical ventilation, continuous renal replacement therapy (CRRT), and prolonged ICU admission compared to patients with blood group O or B.

Such associations have already been reported for pulmonary infection related to severe acute respiratory syndrome coronavirus (SARS-CoV) 1 and 2 [2–5]. However, we would like to comment on these results in light of our data.

Between the 10th of March the 10th of May 2020, we conducted a prospective study involving 172 patients who were consecutively admitted in 6 intensive care units in the University Hospital of Marseille (Assistance Publique des Hôpitaux de Marseille) for a confirmed (RT-PCR) SARS-CoV-2 infection. Admission to the ICU and endotracheal intubation were at the discretion of the attending intensivist for COVID-19 patients. Using our institution database, we collected comorbidities, medications of interest, demographic, clinical, biological, imaging and outcome data.

Most of the infected patients were men ($n = 126$, 73.2%). Average age was 61.9 ± 12.3 years. ABO distribution (O ($n = 54$; 40%), A ($n = 54$; 40%), B ($n = 24$; 18%), and AB ($n = 2$; 1.5%)) was similar to that reported for Hoiland et al. study population. Ninety-six patients (76.1%) had invasive mechanical ventilation at least one week and 29 patients (16.8%) died before three months.

When we compared A/AB patients with O/B patients, we found no statistical differences with SOFA score at admission ($3 [2;7]$ vs. $3 [2;6]$; $p = 0.96$), requirement for mechanical ventilation (78.5% vs. 74.3%; $p = 0.31$), requirement for continuous renal replacement therapy (14.3% vs. 12.8%; $p = 0.50$) and length of stay in ICU (24.8 ± 2.6 vs. 30.7 ± 2.2 days; $p = 0.86$), respectively. As well, biological tests found no statistical differences between A/AB patients with O/B patients regarding white blood cells (8.3 ± 0.5 vs. $7.6 \pm 0.4 \times 10^9/L$; $p = 0.32$), ALT (60.9 ± 6.7 vs. 48.5 ± 5.4 U/L; $p = 0.15$), highest recorded serum creatinine (151.5 ± 31.8 vs. 118.3 ± 26.3 $\mu\text{mol/L}$; $p = 0.42$) and highest recorded serum D-dimer (3.9 ± 0.65 vs. 3.8 ± 2 $\mu\text{g/L}$; $p = 0.42$) at baseline, respectively.

These results are therefore very distinct from those presented by our colleagues, and we discuss some points.

First, one of the most frequently discussed argument of ABO blood typing topic is the different distribution of ABO groups according to local populations, which could influence the results. However, we observed a similar distribution of ABO groups than Hoiland et al. study, and also our ICU cohort's blood group distribution was not different ($p = 0.25$) from the provincial blood group distribution (National French Blood Establishment data: $n = 185\,827$). Furthermore, as our study has pointed out, Latz et al. [6] found that blood type was not associated with risk of intubation or death in patients with COVID-19 acute respiratory distress syndrome. Bing-Bin Wu et al. [7], in a recent meta-analysis, found in the same way no statistical significance in the association between each ABO blood group and COVID-19 severity. In the light of these elements, we could therefore waive local considerations of ABO blood group distribution.

Second, Hoiland et al. present a high proportion of patients requiring continuous renal replacement therapy ($n = 12$, 32%) in the A or AB groups. It has been proven that patients with renal involvement had higher overall mortality compared with patients without [8]. One of the confounding factors that could explain this result might be a difference in treatment protocol between the two groups. Indeed, antiretroviral therapies are implicated in the development of acute renal failure in COVID-19 patients according to the literature [9]. In our cohort, we did not find any treatment protocol differences between A/AB and O/B groups.

Third, one of the pathophysiological explanations reported by the authors is the association between reduced levels of von Willebrand factor that could account as an underlying protective effect against the development of vasculopathy in vital organ vascular beds. As well, we did not find any differences of the amount in von Willebrand factor between A/AB and O/B groups (3.6 ± 0.2 vs. 3.8 ± 0.1 $\mu\text{g/mL}$; $p = 0.61$) to validate this hypothesis.

These results suggest that factors related to ABO blood group type may not be related to the severity of SARS-CoV-2 infection or related-death in our cohort. While there are data regarding the relationship between ABO blood typing and severity of some infectious diseases, studies on COVID-19 are scarce. Further works are needed to explore this hypothetical association between SARS-CoV-2 disease severity and ABO blood group in larger and international prospective cohorts.

Informed consent and patient details

Patients and their relatives were informed of the possibility of the use of medical data for prospective studies and did not manifest opposition. This study was approved by the local Ethics Commission (2020-53) and the French Society of Anaesthesia and Critical Care (00010254-2020-06).

Disclosure of interest

The authors declare no competing financial interests.

Author contributions

D.T. and P.S. contributed to the conception and design of the letter, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. D.T. and J.B. contributed to the acquisition of the data. J.B., D.T. and P.S. contributed to the analysis and interpretation of the data. D.T., J.B. and P.S. contributed to the statistical analyses. All authors participated in manuscript writing, revision and approval for final submission. L.V., D.L. revised the manuscript for critical intellectual content.

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